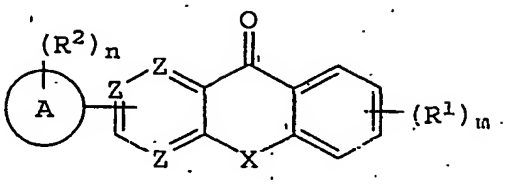
WHAT IS CLAIMED IS:

1. A DNA-PK inhibitor having a formula



or a pharmaceutically acceptable salt thereof,

wherein m is an integer 0 through 3;

n is an integer 0 through 4;

X is O, $S(O)_{0-2}$, or NR^a;

Z, independently, is CR^b or N;

A is heteroaryl or a four- to seven-membered aliphatic ring containing 0, 1, 2, or 3 heteroatoms independently selected from the group consisting of N, O, and S;

R^1, independently, is selected from the group consisting of halo, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocycloalkyl, substituted heterocycloalkyl, $N(R^d)_2$, OR^d, carboxyl, carboxy, nitro, $OC_{1-3}alkyleneN(R^d)_2$, $N(R^d)$-$C_{1-3}alkyleneN(R^d)_2$, $OC_{1-3}alkyleneC(=O)OR^d$, $O(C_{1-3}alkylene)OP(=O)(OR^d)_2$, $O(C_{1-3}alkylene)OP(=O)(ONa)_2$, $OP(=O)(OR^d)_2$, $OP(=O)(ONa)_2$, cyano, aldehyde, carboxamide, thiocarboxamide, acyl, mercapto, sulfonyl, trifluoromethyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or

two R^1 groups are taken together with the atoms to which each is attached to form a 5-, 6-, or 7-membered ring, wherein 1 or 2 carbon atoms of R^1 optionally is a heteroatom selected from the group consisting of O, N, and S, said ring optionally substituted with one or more =O, =S, =NH, OR^c, $N(R^d)_2$, carboxyl, carboxy, alkyl, aryl, substituted aryl, heteroaryl, or substituted heteroaryl, said heteroatom optionally substituted with a group selected from the group consisting of aryl, substituted aryl, alkyl, substituted alkyl, and acyl;

R^2, independently, is selected from the group consisting of OR^d, halo, $N(R^d)_2$, aldehyde, alkyl, substituted alkyl, acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, C_{1-3}alkyleneOR^d, $C(=O)N(R^d)_2$, $N(R^d)_2$, $(C=O)OR^d$, NO_2, $NR^dC(=O)R^d$, $NR^d(SO_2)R^d$, OC_{1-3}alkyleneOR^d, OC_{1-3}alkyleneOC_{1-3}alkyleneR^d, $OC(=O)R^d$, OC_{1-3}alkylene$C(=O)C_{1-3}$alkyleneR^d, and $(SO_3)R^d$;

R^a is selected from the group consisting of hydro, C_{1-4}alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, C_{1-3}alkylenearyl, C_{1-3}alkyleneheteroaryl, C_{1-3}alkyleneheterocycloalkyl, C_{1-4}alkylene-$N(R^d)_2$, C_{1-4}alkyleneOR^d, C_{1-4}alkylene$C(=O)OR^d$, $C(=O)R^d$, $C(=O)N(R^d)_2$, $C(=O)OR^d$, $C(=O)SR^d$, $C(=S)N(R^d)_2$, SO_2R^d, $SO_2N(R^d)_2$, $C(=O)NR^dC_{1-4}$alkyleneOR^d, $C(=O)NR^dC_{1-4}$alkyleneheterocycloalkyl, $C(=O)C_{1-4}$alkylenearyl, $C(=O)C_{1-4}$alkyleneheteroaryl, C_{1-4}alkylene$C(=O)C_{1-4}$alkylenearyl,

C_{1-4}alkyleneC(=O)C_{1-4}alkyleneheteroaryl, C_{1-4}alkylene-C(=O)heterocycloalkyl, C_{1-4}alkyleneNR^{d}C(=O)R^d, C_{1-4}-alkyleneOC_{1-4}alkyleneOR^d, C_{1-4}alkyleneOC_{1-4}alkylene-C(=O)OR^d, and C_{1-4}alkyleneC(=O)N(R^d)$_2$;

R^b, independently, is selected from the group consisting of hydro, alkyl, halo, aldehyde, OR^d, O(C_{1-3}alkylene)OP(=O)(OR^d)$_2$, O(C_{1-3}alkylene)OP-(=O)(ONa)$_2$, OP(=O)(OR^d)$_2$, OP(=O)(ONa)$_2$, nitro, N(R^d)$_2$, carboxyl, carboxy, sulfonamido, sulfamyl, and sulfo or a halide derivative thereof; and

R^d, independently, is selected from the group consisting of hydro, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclo-alkyl, substituted heterocycloalkyl, aryl, C_{1-3}-alkylenearyl, substituted aryl, heteroaryl, and substituted heteroaryl.

2. The inhibitor of claim 1 wherein A is selected from the group consisting of pyridyl, morpholinyl, piperazinyl, thiomorpholinyl, piper-idinyl, and tetrahydropyranyl.

3. The inhibitor of claim 1 wherein m is 0 or 1.

4. The inhibitor of claim 1 wherein n is 0, 1, or 2.

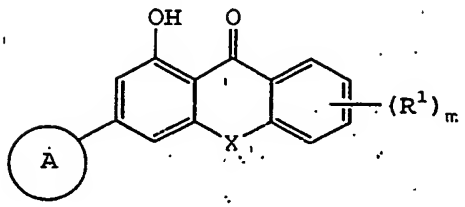
5. The inhibitor of claim 1 wherein X is selected from the group consisting of O, NH, NC(=O)-aryl, NC(=O)alkyl, and NC(=O)heteroaryl.

6. The inhibitor of claim 1 wherein R^1 is selected from the group consisting of halo, OR^d, $OC_{1-3}alkyleneN(R^d)_2$, heterocycloalkyl, substituted heterocycloalkyl, $OC_{1-3}alkyleneC(=O)OR^d$, $N(R^d)C_{1-3}$-alkyleneN$(R^d)_2$, $O(C_{1-3}alkylene)OP(=O)(OR^d)_2$, $O(C_{1-3}alkylene)OP(=O)(ONa)_2$, $OP(=O)(OR^d)_2$, and $OP(=O)(ONa)_2$.

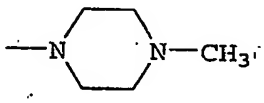
7. The inhibitor of claim 1 wherein n is 0, or R^2 is selected from the group consisting of OH, halo, CH_2OH, $(C=O)NH_2$, NH_2, OCH_3, $NH(C=O)CH_3$, $NHCH_3$, NO_2, $O(CH_2)_{1-3}OH$, O(C=O)heteroaryl, (C=O)aryl, O(C=O)-alkyl, and $OCH_2(C=O)CH_2$aryl.

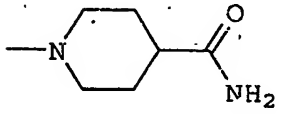
8. The inhibitor of claim 1 wherein Z is CH or C(OH).

9. The inhibitor of claim 1 having a structure



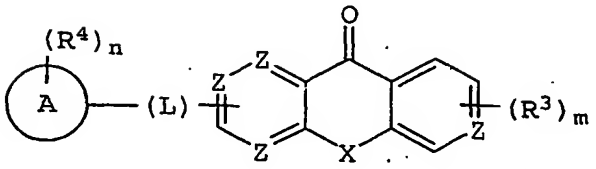
10. The inhibitor of claim 9 wherein m is 0 or R^1 is OCH_3, F,





X is O or NH; and A is morpholinyl.

11. A DNA-PK inhibitor having a formula:



or a pharmaceutically acceptable salt thereof,

wherein m is an integer 0 through 3;

n is an integer 0 through 4;

X is O or NR^a;

Z, independently, is CR^b or N;

L is selected from the group consisting of alkylene, substituted alkylene, carbonyl, carbamoyl, $-NR^d-$, $-N(R^d)_2$, $-O(SO_2)R^d$, $-SO_2R^d$, oxy (-O-), thio (-S-), thionyl (-SO-), and sulfonyl;

A is absent, or A is heteroaryl or a four- to seven-membered aliphatic ring containing 0, 1, 2, or 3 heteroatoms independently selected from the group consisting of N, O, and S;

R^1, independently, is selected from the group consisting of halo, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocycloalkyl, substituted heterocycloalkyl, $N(R^d)_2$, OR^d, carboxyl, carboxy, nitro, $OC_{1-3}alkyleneN(R^d)_2$, $N(R^d)_{1-3}alkyleneN(R^d)_2$, $OC_{1-3}alkyleneC(=O)OR^d$, $O(C_{1-3}alkylene)OP(=O)(OR^d)_2$, $O(C_{1-3}alkylene)OP(=O)(ONa)_2$, $OP(=O)(OR^d)_2$, $OP(=O)(ONa)_2$, cyano, aldehyde,

carboxamide, thiocarboxamide, acyl, mercapto, sulfonyl, trifluoromethyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or

two R^1 groups are taken together with the atoms to which each is attached to form a 5-, 6-, or 7-membered ring, wherein 1 or 2 carbon atoms of R^1 optionally is a heteroatom selected from the group consisting of O, N, and S, said ring optionally substituted with one or more of =O, =S, =NH, OR^c, $N(R^d)_2$, carboxyl, carboxy, alkyl, aryl, substituted aryl, heteroaryl, or substituted heteroaryl, and said heteroaryl optionally substituted with a substituent selected from the group consisting of aryl, substituted aryl, alkyl, substituted alkyl, and acyl;

R^2, independently, is selected from the group consisting of OR^d, halo, $N(R^d)_2$, aldehyde, alkyl, substituted alkyl, acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl C_{1-3}alkyleneOR^d, $C(=O)N(R^d)_2$, $N(R^d)_2$, $(C=O)OR^d$, NO_2, $NR^dC(=O)R^d$, $NR^d(SO_2)R^d$, OC_{1-3}alkyleneOR^d, OC_{1-3}alkyleneOC_{1-3}alkyleneR^d, $OC(=O)R^d$, OC_{1-3}alkyleneC(=O)C_{1-3}alkyleneR^d, and $(SO_3)R^d$;

R^a is selected from the group consisting of hydro, C_{1-4}alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, C_{1-3}alkylenearyl, C_{1-3}alkyleneheteroaryl, C_{1-3}alkyleneheterocycloalkyl, C_{1-4}alkylene-$N(R^d)_2$, C_{1-4}alkyleneOR^d, C_{1-4}alkyleneC(=O)OR^d, $C(=O)R^d$,

$C(=O)N(R^d)_2$, $C(=O)OR^d$, $C(=O)SR^d$, $C(=S)N(R^d)_2$, SO_2R^d, $SO_2N(R^d)_2$, $C(=O)NR^dC_{1-4}alkyleneOR^d$, $C(=O)NR^dC_{1-4}alkyleneheterocycloalkyl$, $C(=O)C_{1-4}alkylenearyl$, $C(=O)C_{1-4}alkyleneheteroaryl$, $C_{1-4}alkyleneC(=O)C_{1-4}alkylenearyl$, $C_{1-4}alkyleneC(=O)C_{1-4}alkyleneheteroaryl$, $C_{1-4}alkyleneC(=O)heterocycloalkyl$, $C_{1-4}alkyleneNR^dC(=O)R^d$, $C_{1-4}alkyleneOC_{1-4}alkyleneOR^d$, $C_{1-4}alkyleneOC_{1-4}alkyleneC(=O)OR^d$, and $C_{1-4}alkyleneC(=O)N(R^d)_2$;

R^b, independently, is selected from the group consisting of hydro, alkyl, halo, aldehyde, OR^d, $O(C_{1-3}alkylene)OP(=O)(OR^d)_2$, $O(C_{1-3}alkylene)OP(=O)(ONa)_2$, $OP(=O)(OR^d)_2$, $OP(=O)(ONa)_2$, nitro, $N(R^d)_2$, carboxyl, carboxy, sulfonamido, sulfamyl, and sulfo or a halide derivative thereof; and

R^d, independently, is selected from the group consisting of hydro, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocycloalkyl, substituted heterocycloalkyl, aryl, $C_{1-3}alkylenearyl$, substituted aryl, heteroaryl, and substituted heteroaryl.

12. The inhibitor of claim 11 wherein A is absent.

13. The inhibitor of claim 11 wherein A is selected from the group consisting of pyridyl, morpholinyl, piperazinyl, thiomorpholinyl, piperidinyl, and tetrahydropyranyl.

14. The inhibitor of claim 11 wherein m is 0 or 1.

15. The inhibitor of claim 11 wherein n is 0, 1, or 2.

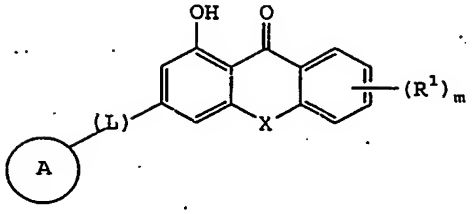
16. The inhibitor of claim 11 wherein X is selected from the group consisting of O, NH, NC(=O)aryl, NC(=O)alkyl, and NC(=O)heteroaryl.

17. The inhibitor of claim 11 wherein R^1 is selected from the group consisting of halo, OR^d, $OC_{1-3}alkyleneN(R^d)_2$, heterocycloalkyl, substituted heterocycloalkyl, $OC_{1-3}alkyleneC(=O)OR^d$, $N(R^d)C_{1-3}$-alkyleneN$(R^d)_2$, $O(C_{1-3}alkylene)OP(=O)(OR^d)_2$, $O(C_{1-3}alkylene)OP(=O)(ONa)_2$, $OP(=O)(OR^d)_2$, and $OP(=O)(ONa)_2$.

18. The inhibitor of claim 11 wherein R^2 is selected from the group consisting of OH, halo, CH_2OH, $(C=O)NH_2$, NH_2, OCH_3, $NH(C=O)CH_3$, $NHCH_3$, NO_2, $O(CH_2)_{1-3}OH$, O(C=O)heteroaryl, (C=O)aryl, O(C=O)alkyl, and $OCH_2(C=O)CH_2$aryl.

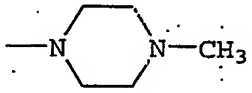
19. The inhibitor of claim 11 wherein Z is CH, C(OH), $COCH_2CH_2OP(=O)(OCH_2C_6H_5)_2$, $COCH_2CH_2OP$-$(=O)(ONa)_2$, $OP(=O)(OCH_2C_6H_5)_2$, and $OP(=O)(ONa)_2$.

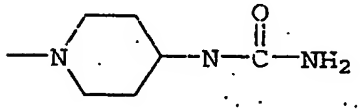
20. The inhibitor of claim 11 having a structure



and prodrugs thereof.

21. The inhibitor of claim 19 wherein m is 0 or R^1 is OCH_3, F,





X is O or NH; and A is absent.

22. A DNA-PK inhibitor selected from the group consisting of:
trifluoromethanesulfonic acid 1-hydroxy-9-oxo-9H-xanthen-3-yl ester;
1-hydroxy-3-morpholin-4-yl-xanthen-9-one;
1-hydroxy-6-methoxy-3-trifluoromethanesulfonylxanthen-9-one ester;
1-hydroxy-6-methoxy-3-morpholin-4-yl-xanthen-9-one;
6-fluoro-1-hydroxy-3-morpholin-4-yl-xanthen-o-one;
1-hydroxy-6-(4-methylpiperazin-1-yl)-3-morpholin-4-yl-xanthen-9-one;
1-(8-hydroxy-6-morpholin-4-yl-9-oxo-9H-xanthen-3-yl)-piperidine-4-carboxylic acid amide;
trifluoromethanesulfonic acid 1-hydroxy-9-oxo-9,10-dihydro-acridin-3-yl ester; and
1-hydroxy-3-morpholin-4-yl-10H-acridin-9-one.

23. A pharmaceutical composition comprising (a) DNA-PK inhibitor claim 1 or claim 11, and (b) a pharmaceutically acceptable carrier or diluent.

24. A pharmaceutical compcsition comprising (a) a DNA-PK inhibitor of claim 1 or 11, and (b) an antineoplastic agent.

25. The pharmaceutical composition of claim 24, wherein A is morpholinyl, L is absent, R^1 and R^2 are hydrogen, and Z is CH at each occurrence.

26. The pharmaceutical composition of claim 24 wherein L is absent, or L is selected from the group consisting of $-NR^d-$, and -S-;

A is absent, or is selected from the group consisting of morpholinyl, piperazinyl, thiomorpholinyl, piperidinyl, and tetrahydropyranyl;

m is 0 or 1, or R^1 is selected from the group consisting of halo, OR^d, $OC_{1-3}alkyleneN(R^d)_2$, heterocycloalkyl, substituted heterocycloalkyl; $OC_{1-3}alkyleneC(=O)OR^d$, $N(R^d)C_{1-3}alkyleneN(R^d)_2$, $OP(=O)-(OR^d)_2$, and $OP(=O)(ONa_2)$; and

n is 0, 1, or 2, or R^2 is selected from the group consisting of OH, halo, CH_2OH, $(C=O)NH_2$, NH_2, OCH_3, $NH(C=O)CH_3$, $NHCH_3$, NO_2, $O(CH_2)_{1-3}OH$, $O(C=O)$heteroaryl, $(C=O)$aryl, $O(C=O)$alkyl, and $OCH_2(C=O)-CH_2$aryl.

27. The pharmaceutical composition of claim 24 wherein the antineoplastic agent comprises a chemotherapeutic agent or a radiotherapeutic agent.

28. The pharmaceutical composition of claim 27 wherein the antineoplastic agent is selected from the group consisting of an alkylating agent, an antimetabolite, a type I topoisomerase inhibitor, an antimitotic drug, an antibiotic, an enzyme, a biological response modifier, a differentiation agent, and a radiosensitizer.

29. The pharmaceutical composition of claim 27 wherein the antineoplastic agent is selected from the group consisting of mechlorethamine, cyclophosphamide, ifosfamide, melphalan, carmustine, chlorambucil, lomustine, semustine, thriethylene-melamine, triethylene thiophosphoramide, hexamethylmelamine, busulfan, dacarbazine, methotrexate, trimetrexate, 5-fluorouracil, fluorodeoxyuridine, gemcitabine, cytosine arabinoside, 5-azacytidine, 2,2-difluorodeoxycytidine, 6-mercaptopurine, 6-thioguanine, azathioprine, 2'-deoxycoformycin, erythrohydroxynonyladenine, fludarabine phosphate, 2-chlorodeoxyadenosine, camptothecin, topotecan, irinotecan, paclitaxel, vinblastine, vincristine, vinorelbine, docetaxel etoposide, teniposide, actinomycin D, daunomycin, doxorubicin, mitoxantrone, idarubicin, bleomycin, plicamycin, mitomycin C, dactinomycin, L-asparaginase, interferon-alpha, IL-2, G-CSF, GM-CSF, metronidazole, misonidazole, desmethylmisonidazole, pimonidazole etanidazole, nimorazole, RSU 1069, EO9, RB 6145, SR4233, nicotinamide, 5-bromodeozyuridine, 5-iododeoxyuridine, bromodeoxycytidine, cisplatin, carboplatin, mitoxantrone, hydroxyurea, N-methylhydrazine, procarbazine, mitotane, aminoglutethimide, prednisone, dexamethasone, hydroxyprogesterone caproate, hydroxyprogesterone acetate, megestrol acetate, diethylstilbestrol ethynyl estradiol, tamoxifen, testosterone

propionate, fluoxymesterone, flutamide, leuprolide, flutamide, tin etioporphyrin, pheoboride-a, bacteriochlorophyll-a, a naphthalocyanine, a phthalocyanine, and a zinc phthalocyanine.

30. A method of inhibiting DNA-PK activity comprising the step of contacting a DNA-PK with a DNA-PK inhibitor of claim 1 or 11.

31. A method of sensitizing a cell type to an agent that induces DNA lesions comprising the step of contacting the cell type with a compound of claim 1 or 11.

32. The method of claim 31 wherein the agent that induces DNA lesions is selected from the group consisting of radiation, an exogenous chemical, a metabolite by-product, and mixtures thereof.

33. A method of potentiating a therapeutic regimen for treatment of a cancer comprising the step of administering to an individual in need thereof an effective amount of a DNA-PK inhibitor of claim 1 or 11.

34. The method of claim 33 wherein the therapeutic regimen for treatment of cancer is selected from the group consisting of chemotherapy, radiation therapy, and a combination of chemotherapy and radiation therapy.

35. A method of characterizing the potency of a test compound as an inhibitor of a DNA-PK polypeptide, said method comprising the steps of:

a) measuring an activity of a DNA-PK polypeptide in the presence of a test compound;

b) comparing the activity of the DNA-PK polypeptide in the presence of the test compound to the activity of the DNA-PK polypeptide in the presence of an equivalent amount of a reference compound of claim 1 or 11, wherein a lower activity of the DNA-PK polypeptide in the presence of the test compound than in the presence of the reference compound indicates that the test compound is a more potent inhibitor than the reference compound, and a higher activity of the DNA-PK polypeptide in the presence of the test compound than in the presence of the reference compound indicates that the test compound is a less potent inhibitor than the reference compound.

36. A method of characterizing the potency of a test compound as an inhibitor of a DNA-PK polypeptide, said method comprising the steps of:

a) determining an amount of a control compound of claim 1 or 11 that inhibits an activity of a DNA-PK polypeptide by a reference percentage of inhibition, thereby defining a reference inhibitory amount for the control compound;

b) determining an amount of a test compound that inhibits an activity of a DNA-PK polypeptide by a reference percentage of inhibition, thereby defining a reference inhibitory amount for the test compound;

c) comparing the reference inhibitory amount for the test compound to a reference inhibitory amount determined according to step (a) for the control compound, wherein a lower reference inhibitory amount for the test compound than for the control compound indicates that the test compound is a more potent inhibitor than the control compound, and a higher reference inhibitory amount for the test compound than for the control compound indicates that the test compound is a less potent inhibitor than the control compound.

37. The method of claim 36 wherein the method comprises determining the reference inhibitory amount of the test compound in an *in vitro* biochemical assay.

38. The method of claim 37 wherein the method comprises determining the reference inhibitory amount of the test compound in an *in vitro* cell-based assay.

39. The method of claim 36 wherein the method comprises determining the reference inhibitory amount of the test compound in an *in vivo* assay.

40. An article of manufacture comprising:

a) an anticancer compound that induces double-strand DNA breakage in cells; and

b) a package insert describing a coordinated administration to a patient of said anticancer compound and a DNA-PK inhibitor compound of claim 1 or 11.

41. The article of manufacture according to claim 40 wherein said anticancer compound induces DNA double strand breaks.

42. The article of manufacture according to claim 40 wherein the anticancer compound is selected from the group consisting of bleomycin and etoposide.

43. An article of manufacture comprising:

a) a compound selected from the group consisting of a cytokine, a lymphokine, a growth factor, and a hematopoietic factor; and

b) a package insert describing a coordinated administration to a patient of said compound and a DNA-PK inhibitor compound of claim 1 or 11.

44. An article of manufacture comprising:

a) a pharmaceutical composition comprising a DNA-PK inhibitor of claim 1 or 11 in a pharmaceutically acceptable carrier; and

b) a package insert describing a therapeutic treatment comprising administering the DNA-PK inhibitor.

45. An article of manufacture comprising:

a) a pharmaceutical composition comprising a DNA-PK inhibitor of claim 1 or 11 in a pharmaceutically acceptable carrier; and

b) a package insert describing a therapeutic treatment comprising administering the DNA-PK inhibitor.